



# BIBLIOGRAPHY OF HOOKWORM DISEASE

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## PREFACE

When in 1910 the newly organized Rockefeller Sanitary Commission began to assist the Southern States in measures for the control of hookworm infection, it soon became evident that a considerable amount of information on this disease was already available in the literature, which needed to be made more readily accessible. With the organization of the International Health Board in 1913 and the broadening of the program of hookworm control to include foreign countries this need became even more apparent. One of the first steps of the new Board, therefore, was to undertake the preparation of a bibliography which is now published in order to put it at the service of hygienists and all others who are interested.

Emphasis has been laid, in the compilation of the volume, on the social and economic aspects of the disease and the efforts to control it, rather than on the biology of the parasite. It is believed that the volume contains almost all of the references that can be verified in the United States. Such of the material as remains unpublished (represented by the entries preceded by asterisks) may be consulted in the library of the Rockefeller Foundation.

. A large part of the literature of hookworm disease is controversial in character. This is due, as the historical introduction to the present volume points out, to the fact that discussion, centering mainly around various practical problems connected with the control of the disease, has been carried on under a great variety of difficult conditions which permitted little opportunity for the kind of scientific investigation necessary to settle the points at issue.

Tabulation of the 5,680 entries appearing in this volume indicates four peaks of activity in the production of literature on hookworm disease: the first occurs in 1882, just after the disease had wrought havoc among the workers in the Saint Gotthard tunnel; the second in 1903, when general alarm was felt over its spread in European mines; the third in 1910, when a period of scientific activity culminating in the publication of Looss's monograph in 1911 was drawing to a close; and the fourth in 1917, just before America's entry into the World War, when activity in combating the disease in many of the tropical and semi-tropical countries was at the height.

The bibliography could not have been compiled without the co-operation of many libraries. Special acknowledgment is hereby made of cordial and effective assistance rendered by the library of the Surgeon General of the United States Army, the library of the New York Academy of Medicine, the New York Public Library, and the library of the United Engineering Societies.

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#### INTRODUCTION

The hookworm was not discovered until 1838, but attempts have been made to trace the disease back to ancient times. Certain statements in a manuscript of 1550 B.C. are interpreted by many authorities as indicating that both the hookworm and hookworm disease were known to the ancient Egyptians. This interpretation was strongly opposed by F. von Oefele (1901), who studied the original papyrus text. Arthur Looss, the eminent authority on hookworm disease, most of whose work was done in Cairo, believes that von Oefele's views are plausible, and concludes: "It is thus only negatively probable that the arcient Egyptians should have known the Ankylostoma as a distinct animal and as the cause of a definite disease, although both the parasite and the disease were no doubt frequent in ancient times."

Through the records of ancient history run accounts of epidemics of anemia that may reasonably be suspected of having had some connection with the hookworm. Hippocrates, about 440 B.C., draws a suspicious clinical picture of a disease that caused people to eat stones and earth, brought upon them great intestinal disturbances, and, though it was not jaundice, gave people much the same color as did the latter disease. In classical literature the striking pallor of miners is frequently mentioned, appearing, for example, in the works of Lucretius and Lucan (50 B.C. and 50 A.D.). At that time it was the custom to accuse gold of giving off evil exhalations which soon turned the greedy delvers the same color as the metal they sought. No one suspected the existence of the anemia-producing hookworm.

Certain "round worms" mentioned in an Arabian manuscript by Avicenna have been identified as hookworms, and the symptoms caused by these worms, which Avicenna traced in considerable detail, are apparently those of hookworm disease. Dr. Khalil, who discusses the manuscript and translates sections of it in a recen, number of the Journal of Tropical Medicine and Hygiene, thinks this is probably the earliest valid record of Ancylostoma and Ancylostomiasis. During the last three centuries reports have become fairly definite. Piso (1611–1678) in Brazil, Father Labat (1663–1738) in Guadeloupe, and Bryan Edwards (1743–1800) in Jamaica, all describe epidemics of a disease then known under various names, such as anemia, dropsy, intestinal disturbance, and weakness. It was particularly noticed as a cause of death among negro slaves. The symptoms coincide with those of hookworm disease. A great

deal of misinterpretation has continued down to recent times, especially as regards the relation of malaria to anemia, and as to the correct cause of dirt-eating and other symptoms supposedly caused by warm climates.

Before the hookworm was finally found in man a number of related species were discovered in animals. In 1782 Goeze found some worms in the intestines of a badger (*Meles taxus*), which, on account of their hair-like shape, he called *Ascaris criniformis*, though he suspected them of belonging to a genus different from that of the ordinary Ascaris. He noted a membranous expansion of the tail of the male, with two rib-like structures in it which he called hooks. In 1789 similar worms were found in the intestines of foxes by Froelich. He also observed the membranous expansion and the so-called hooks, and therefore gave the name *Haakenwurm* ("hookworm," or *Uncinaria*) to the genus. These animal parasites were species of the hookworm, but not the same species that are harbored by man.

## Discovery of the Hookworm

Of the two main species of hookworm which infest man—the Ancylostoma duodenale and Necator americanus—the former was the first to be discovered. Worms of this species were recognized in 1838 by Angelo Dubini, an Italian physician, who found them in the body of a peasant woman who had died of pneumonia in the hospital at Milan. They were encountered a second time at an autopsy in December, 1842. The latter finding led to a systematic examination of one hundred bodies, in twenty of which the parasites were discovered. In 1843 Dubini published a detailed account of the worm, to which he gave the name Agchylostoma duodenale. He noted the true hooks, the four hook-like teeth that stand out from the rounded mouth. Thereafter he continued to come across further specimens, which, as he remarked, were easily found if a proper search were made. The reason these common intestinal parasites had not before been found, he attributed to the imperfect manner in which earlier autopsies had been performed.

Dubini gave a description of the physical aspect of hookworms, but he did not emphasize the harm that they can do to the human system. Although he suspected that the body was not unaffected by their presence, he reported that the mucous membrane to which they attach themselves looked normal, or at worst "arborescent," and that he was unable to name any special symptoms produced by the worms. The individuals harboring the parasites had died from a variety of causes, and it seemed impossible to ascribe any one of the deaths to hookworm infection.

Von Siebold in 1845 classified the hookworm as belonging to the Strongyloidae. Soon afterward, Castiglioni described the occurrence of hookworms in the bodies of dropsical and cachectic individuals, but, like Dubini, did not realize their pathogenic importance.

Scientists elsewhere soon began to connect the parasite with certain diseases, chief among which was Egyptian chlorosis. In 1847 Pruner, while making autopsies, had found the worm in Egypt. Bilharz (1853) and Griesinger (1854) connected the parasites with the extremely prevalent chlorosis which was the cause of more than one fourth of all the deaths in that country. Griesinger was emphatic enough in his statements, but the physicians in Egypt paid little attention to him. Twenty years later most of them remembered only vaguely his work or that of Pruner and Bilharz.

But in other parts of the world the work of Griesinger had a stimulating effect. In Brazil, Wücherer in 1866 found hookworms in the bodies of patients who had died from tropical anemia, and subsequent observations by Brazilian physicians confirmed the suspicion that the parasites were responsible also for this widely prevalent disease. These and other similar studies resulted in the parasite discovered by Dubini being established in the minds of medical men as the cause of a severe anemia found almost everywhere in tropical regions.

# Origin of Fecal Diagnosis

Until 1877 the hookworm had been found only at autopsy. A simple method for diagnosing hookworm infection in living beings was wanting. This was supplied as a direct result of extensive research in Italy. In a paper written in 1878 Grassi and two brothers, Ernesto and Corrado Parona, demonstrated that hookworm disease could be recognized from ova passed in the feces. From that date forward it became the custom to search for hookworm eggs in the feces of anemic patients, with the result that constantly increasing numbers of patients of this class were found to be hookworm carriers.

# The Saint Gotthard Epidemic

Hookworm disease was still a comparatively unknown malady in 1880, when the Saint Gotthard tunnel was under construction. Though this tunnel was not located in Italy, the men working on it were chiefly Italians; hence, when a violent epidemic of anemia developed among them, the Italian government concerned itself with their welfare and sought and obtained from the Swiss government official information concerning the outbreak.

The first cases were recognized in February, 1880, just a year before the tunnel was completed. Hundreds of cases were soon verified, and all Italy became alarmed. There was much agitation in the press, both scientific and popular. The new method of diagnosis placed the helminthologists of northern Italy in an excellent position to demonstrate that the sufferers harbored hookworms. Of this fact there was no question, but as to whether the worms actually produced the disease there was much diversity of opinion. Some among a number of Italian physicians who went to the Saint Gotthard tunnel to investigate the malady were inclined to hold the adverse hygienic conditions responsible for the bad health of the men. The only scientist who steadily insisted on the parasitic origin of the anemia was Edoardo Perroncito, then professor of pathology at the veterinary school of the University of Turin.

Perroncito, who was present at the first postmortem examination made by Colomiatti, in which 1,500 worms were found in the body of a laborer who had died from anemia while working at the tunnel, immediately began extensive studies of the hookworm. Gradually, through tireless effort and demonstration, he won others to his views. Proof that the anemia could be cured by vermifuges that expelled the hookworms was the chief factor that converted leading Italian medical men, although in other places, especially in France, the bold conclusion that miners' anemia the world over was due to hookworms continued to find a great deal of opposition. After 1895 the quarrel died down, and eventually Manouvriez and Fabre, mining physicians of international reputation, were converted to the view that miners' anemia was due to hookworms. Thus had Perroncito succeeded in gaining general support for his original hypothesis.

## Development of Vermifuges

Experiments with drugs for removing hookworms from the body had been carried on before the Saint Gotthard epidemic, but without satisfactory results. Bozzolo and Pagliani, in their report on the Saint Gotthard tunnel in 1880, confessed that "no method is known at present for killing, rendering inactive, or expelling hookworms. All known anthelmintic remedies have been tried without success." The urgent need of a vermifuge was recognized. Perroncito and Bozzolo, both members of the Turin Academy of Medicine, were prominent in the discussion, and the two became eager rivals in the search for an effective drug.

Perroncito, who had observed the enormous resistive power to most chemical agents that hookworm larvae possessed, nevertheless noted that in a one-half-of-one-per-cent solution of thymol immature larvae died immediately, while mature larvae lived only eight to ten minutes. In a well-prepared extract of male-fern (Extractum Filicis Maris Aethereum), mature larvae died even more quickly—in from five to ten minutes. This led to a trial of the drug, followed by Perroncito's announcement that by repeated administration of fresh extract of male-fern he had succeeded in reducing the number of hookworms harbored by two patients, though he pointed out the futility of expecting one or two doses of the drug to remove all hookworms from the intestine.

This announcement by Perroncito was also received with considerable scepticism. Bozzolo stated that his studies of vermifuges had yielded negative results, and that it was better to stress prophylaxis; Concato proposed giving up the idea of killing the parasite, thinking it better to stress attempts at building up the system; and Bizzozero thought the transfusion of blood into the peritoneal cavity might restore the patients' health. But in spite of the adverse comment, Perroncito's method of treatment was taken up in certain parts of Italy; cures were reported; and eventually the Italian government began to use male-fern in treatments given at government expense.

Bozzolo, in 1879, had tried thymol as a vermifuge for hookworm anemia among the brickmakers in northern Italy, but the doses used were too small to be effective. Later he increased the dose, and in 1881 announced that he had succeeded in curing six patients, some of whom could not tolerate malb-fern. Lutz, in Brazil, immediately began the use of the drug, and in 1883 pronounced it preferable to male-fern. Gradually it came into favor in Italy and elsewhere, until, in an article written in 1912, Bozzolo was able to give an extended account of the success with which it had been used throughout the world.

#### Hookworm Disease in Mines

From the Saint Gotthard tunnel, which was completed in 1882, hookworm disease spread over Europe. The tunnelers sought work in European mines, and seemed to revive an epidemic of the malady that had existed in these mines, at intervals, for centuries. The disease became most severe in the sulphur mines of Sicily; in the gold and silver mines of Hungary; in the coal mines of Germany, Holland, Belgium, and France; in the lead mines of Spain; and in the tin mines of England.

In Germany an energetic campaign conducted from 1903 to 1914, was attended with striking results, reducing the rate of infection, which had reached the high point of 13.1 per cent in 1903, to 0.17 per cent in 1914. Infected miners were treated, new employes who carried hookworms were excluded from underground work, sanitary conveniences were introduced;

and all of these measures were strictly enforced. As the rate of infection was reduced, the work of examining underground miners decreased, but the reverse was true of the examination of applicants for employment. The latter activity assumed such vast proportions that several million microscopic examinations were made from 1903 to 1913.

An illuminating discussion preceding the campaign produced, from 1896 to 1903, a considerable body of literature in Germany. Questions of fundamental policy were discussed; physicians took sides; the daily press became interested; and ultimately both the Prussian Diet and the Imperial Reichstag concerned themselves repeatedly with the problem. In 1903 the controversy ended with a victory for the sponsors of an extensive and thorough hygienic program.

In Belgium the methods employed were about the same as those in Germany, with the marked exception that coercion by government was replaced by co-operative effort developed through educational work among the men, about 35 per cent of whom were illiterate. In the Liége district, where the disease was most severe, the rate of infection was reduced from 22.8 per cent in 1902 to 1.2 per cent in 1913. The result was achieved chiefly through treatment, little progress being made in installing sanitary conveniences.

Prompt action on the part of the Dutch government, before the disease had become severe in the mines of that country, permitted the campaign to be largely prophylactic, mild, and comparatively inexpensive, instead of curative, drastic, and expensive, as in Germany and Belgium. Results were secured by co-operative effort in which the mine-owners splendidly performed their part. The rate of infection was reduced from 25.1 per cent in 1904 to 0.3 per cent in 1913.

Interest in France was aroused by alarming reports concerning the spread of hookworm disease in the mines of Belgium and Germany. An invasion was feared. A survey made in 1904 disclosed a varying amount of infection in the mine districts, but the situation was considered by no means alarming. In 1911 certain sanitary laws were passed and treatment was provided at the expense of the mining companies, with compensation for time lost from labor. No systematic campaign was conducted.

In Italy the workers in the Sicilian sulphur mines bore the brunt of the disease. It was discovered here as early as 1882. A survey in 1898 revealed an infection of about 50 per cent, but no campaign was undertaken. Another investigation in 1912 indicated that conditions had grown worse rather than better. In 1914 an experimental campaign was begun in two Sicilian mines and a considerable reduction in infection was brought about, chiefly by means of treatment. Some work was also done in a small

sulphur-mining center in the Romagna, on the Italian mainland, where a campaign of disinfection and treatment is said to have decreased the incidence of the disease from 38.2 per cent in 1908 to 0.3 per cent in 1914.

Conditions in Austria were not favorable for the development of the parasite, owing largely to the dryness of the mines. English mines, too, were for the most part exempt, except the tin mines in Cornwall and Devon, where sporadic work in examining the men was undertaken and some sanitary reforms were introduced, though the infection was never serious enough to call for drastic action.

At present Hungary and Spain are centers of the most severe mine infection in Europe. Certain Hungarian mining sections which have been infected for centuries are still a standing menace, although in one section (Brennberg) heroic efforts have been made to stamp out the disease. In Spain very little has been done. The rate of infection appears to be highest in the lead mines of Linares, where it ranges from 50 to 90 per cent and where conditions are in every way favorable for the further spread of the disease.

The infection in a mild form is also found among the non-mining population of certain European countries. Thus, it has been discovered among brickmakers in Holland and Germany, and cases from tropical countries are occasionally imported into England. But the climate of the northern European countries is too cold for the hookworm to propagate extensively on the surface. Except underground, widespread infection is present only in Italy and perhaps in certain sections of southern Russia and the Balkan states. In Italy it is found on the surface in brick-yards, truck farms, and rice-fields, and in general among people whose work brings them into contact with the soil. Except for thorough discussion and an attempt to get the state to manufacture thymol, little has been done in Italy to control the disease, although the harm it works to agricultural interests has been repeatedly pointed out.

# Discovery of Dermal Infection

Many conflicting views were originally held as to the process by which human beings acquired the infection. One of the earliest was the belief that hookworm larvae might be transported by air currents or in dust. Experiments made by von Schopf in Hungary about 1888 apparently confirmed this view, which arose indirectly from Perroncito's erroneous theory that desiccated mature hookworm larvae revived if placed in a moist medium, and was not finally overthrown until a great deal of controversial matter had been published.

The part played by animals, especially the horse, in the distribution of hookworm disease, also gave rise to discussion, and in some of the mines of Hungary horse-haulage was discontinued. Increased experimentation has, however, made it seem extremely unlikely that any domestic animals are carriers of either Ancylostoma duodenale or Necator americanus. The species of hookworms found in domestic animals differ from the human hookworms and, with the single exception of Ancylostoma ceylanicum, which is parasitic to the dog and has been found in small numbers in East Indians, they do not inhabit the human body.

It was at first thought that the worms could enter the body only by way of the mouth, being acquired in the main from contaminated food. That this mode of entry was possible was shown provisionally by Leuckart in 1866 and proved experimentally by Leichtenstern in 1887. But in 1898 Arthur Looss, professor of parasitology at the government medical school at Cairo, accidentally discovered that a hookworm culture spilled on his hands produced dermatitis. Later, when he found hookworm ova in his feces, he concluded that he had been infected through the skin. succeeding years he proved experimentally his theory of dermal infection, according to which hookworms in their larval stage may enter the human body through the skin-at any place, but preferably between the toes, or wherever else the skin is tender. His communications on the subject aroused a great deal of criticism, but in the end his views not only as to the acquisition of infection through the skin but also concerning the intricate migratory path of the hookworm larva after it enters the human body were established in every detail.

This discovery revolutionized methods of control. Measures were henceforth directed toward avoiding contact between the bare skin and infected mud or water. Warnings against going barefoot and against leaky or wet shoes superseded those against contaminated food. All writers now agreed that the most common and only important mode of infection was by way of the skin.

#### Close of a Period

The period of research and investigation which opened so brilliantly with the discoveries at the Saint Gotthard tunnel, culminated in 1911 in the publication of Looss's monograph on the hookworm, in which all the scientific knowledge of the parasite then available was carefully summarized and much new light shed on its life-cycle and anatomy. During the period following the construction of the Saint Gotthard tunnel—that is, from about 1880 to 1898—according to Zinn and Jacoby, who collected the literature, some 500 papers appeared on the hookworm, on hookworm

infection, and on hookworm control; by 1905, about 250 other papers had been added; and in 1911, after an uninterrupted stream of magazine articles and studies had borne witness to the sustained interest in the subject, Looss's monumental volume was published.

The main facts about the life of the hookworm were now clear. Successful experimental campaigns against the disease had been undertaken in the mines of several European countries, and the danger of a new occupational disease that had threatened to cripple the mining industry had been averted. Thymol and male-fern were accepted as established remedies. The time was now ripe for an incursion into the stronghold of the parasite, the tropical and semi-tropical lands where it thrives and does its greatest damage. But some years before this the principal scene of activity had shifted to America, where effective machinery for carrying the fight into the tropics had been developed and tested.

#### Discovery of the Necator Americanus

In 1808 Joseph Pitt, in an article on dirt-eating and anemia among the lower-class negro and white population of the South, ascribed the symptoms to deficiency in nourishment. Thereafter periodic discussions occurred, but apparently none of the writers suspected that they were dealing with a disease that was both widespread and communicable. Few of the descriptions gave anything like an adequate picture of the symptoms. The disease was regarded with grave concern chiefly because of the mortality it produced among the slaves. Thus, one of the best of the early accounts, printed in 1820 by James Thomson, describes the havoc it wrought among slaves in Jamaica.

But it was not until 1893 that Blickhahn, of St. Louis, reported what appears to have been the first case recognized as hookworm disease in the United States. The infection was probably caused by Ancylostoma duodenale, as the patient was a brickmaker from Westphalia. Soon other endemic as well as imported cases were noted, chiefly in Texas; and from 1896 on, an increasing number of cases were reported from various parts of the country. Close study revealed that they were caused by a heretofore undescribed species of hookworm.

On May 10, 1902, Dr. Charles Wardell Stiles, zoologist, of the United States Bureau of Animal Industry, described the new species of hookworm and named it the *Uncinaria americana*, or *Necator americanus* (Stiles). The worms had been noted before—for example, by Lutz in Brazil in 1888—but Stiles was the first to recognize that they were of a distinct species. His work, though based in part on a study of specimens sent from Porto Rico by Ashford, was also greatly aided by a case described

by Allen J. Smith in 1901 and another by T. A. Claytor in the same year. About the same time Claude A. Smith and H. F. Harris were reporting cases from Georgia, and a little later Harris surmised that much of the anemia in certain southern states was due, not to malaria, as had been previously thought, but to hookworm disease. Stiles's work left no longer any doubt that there were extensive areas in the United States in which existed severe hookworm disease produced by the new type of worms.

It was also shown that the newly discovered American hookworm was being carried to Europe, chiefly through seasonal immigration. Thus, when Italian workmen returned to Italy after working a part of the year on Brazilian coffee plantations, they took back with them worms of the new-world variety, with the result that most of the infection in Italy, outside of the mines, was caused by worms of the American species. (In this connection it may be interesting to note that these worms, although called "the American hookworm" from the name Necator americanus and from the fact that they were first described in America, are in reality as much an old-world hookworm as the Ancylostoma duodenale. Their original habitat was probably Africa, whence they were doubtless carried to the New World by the importation of negro slaves.)

A very gradual awakening to the importance of hookworm disease in the United States followed the 1902 discoveries. Meanwhile, important work was going forward in Porto Rico. For years preceding the occupation of this island by the United States, the extremely prevalent and fatal anemia had been much discussed, but it was not until 1899, the year following the American occupation, that Dr. Bailey K. Ashford, of the United States Army, correctly ascribed the hookworm as the cause of this anemia. Dr. Ashford was then in charge of a large field hospital sheltering the victims of the cyclone that occurred in August of that year. He carefully studied some of the patients, and gave a detailed and accurate description of the disease, in which he stressed its economic aspect. In 1902, after a study of the literature in the Surgeon General's library, Ashford returned to Porto Rico and, with Walter W. King, of the United States Public Health and Marine Hospital Service, undertook a complete investigation of 100 cases. In an article resulting from this study he announced that in his opinion over 30 per cent of the deaths in Porto Rico were due to this anemia, and lodged an earnest appeal for a campaign against it.

In 1904 the legislature of Porto Rico appropriated \$5,000 for the study and treatment of anemia, and Doctors Ashford, King, and Guiteras were made members of a commission to have charge of the campaign, the services of the two first-named physicians being contributed by the United States War and Treasury departments, respectively. Since then the work

of combating hookworm disease in this island has gone steadily forward in spite of difficulties, with responsibility being gradually transferred to the local authorities. Soon after the Porto Rican campaign got under way, preparations began to be made for coping with the same problem in the United States.

# The Campaign Against Hookworm in the United States

The period between 1910 and 1913 was marked by the entrance of various state boards of health into the fight. These were assisted in their work by voluntary health organizations, one of the first of which was the Rockefeller Sanitary Commission, established in 1909 for the purpose of combating hookworm disease. In 1915 the work of this organization was merged with that of the International Health Board—one of the agencies through which the Rockefeller Foundation, founded in 1913, carries on its work. Much of the effort of this Board has been directed toward promoting measures for the control of hookworm disease.

Concerted efforts against hookworm disease in the United States were started by sanitary and infection surveys in eleven southern states, followed by a campaign of cure and prevention. The infection survey, covering chiefly rural children between six and eighteen years of age, confirmed the presence of hookworm disease in every one of the 700 countles investigated, and indicated that soil pollution was chiefly responsible for the evil. The surveys demonstrated to the country at large, as well as to the Southern States, that hookworm disease was a reality and a serious menace to health and prosperity. Aroused to the importance of this hitherto neglected disease, many Southern physicians published papers on it, and the state boards issued bulletins. This attitude was in marked contrast to that of 1910, when newspapers were fond of regaling their readers with discussions in which the infection was referred to in such terms as "the lazy germ," "the hookworm theory," "the fad," "the myth," and "the conception of ingenious minds for the injury of the South." At that time many denied the presence of the disease in the South, and some professed not to believe in its existence anywhere. Few newspapers could be said to be friendly, or willing to co-operate in the efforts to stamp out the infection. But as knowledge advanced and progress was made in locating infected persons, the papers changed their attitude one by one and began to publish more serious references to the disease. Eventually they became warm supporters of the health workers in the task of educating the public. By 1914 they had been completely won over, and, realizing now the importance of the disease, were glad to give their whole-hearted support to the campaign against it.

Medical schools in several states also began to provide instruction in the diagnosis and treatment of intestinal parasites as a requirement for graduation, Tulane University, in particular, adopting a high standard of instruction in the subject. The effort to impress upon school children the relationship between clean soil and good health, as part of the regular instruction in public schools, also met with success, the educational departments of states and counties becoming strong allies in promoting the cause of sanitation. The United States Public Health Service interested itself extensively in the technical side of hookworm control, and under the direction of Dr. Charles Wardell Stiles conducted much valuable research work and many special surveys; while in the state of California, also, a variety of agencies, including the State Board of Health and the United States Bureau of Mines, did much important work on hookworm disease in mines.

The field work undertaken for the relief and control of the disease centered at first in the free traveling dispensary, where examination and treatment were given to all who applied. These dispensaries, visiting at weekly intervals various convenient points throughout the counties, paved the way for a more intensive type of organization which subsequently, by house-to-house canvass, carried the work into every corner of selected communities. It was found that by confining attention to a small rural community of 500 or 600 people, a medical field director with trained assistants could treat within a short time practically every infected person and could also secure a great reduction in soil pollution. As the work expanded it became possible by 1916 to cover an entire county in approximately one year, using a working force of standard size, consisting of the medical field director and three to five health inspectors.

The work of combating hookworm disease in a given territory involved mapping the district, taking a census of the population, numbering the houses, making microscopic examination of fecal specimens for the entire population, treating those found infected, and continuing microscopic examination until cure was effected. Coincidently with examination and treatment of the people the attempt was made to secure the installation and use of latrines at all the homes.

Much emphasis was placed on the use of properly constructed latrines as a means of protection against typhoid fever and dysentery as well as against hookworm disease. The scientific aspects of the latrine problem also received attention, many sanitarians studying the relative efficiency of various types of latrines as a means of preventing hookworm and the other soil-borne intestinal infections. Various approved types of latrines were worked out and put into use, the exact type recommended being determined in each case by the local department of health.

## Extension of Hookworm Work to Many Parts of the World .

The activities in the southern part of the United States led to the extension of hookworm control effort to other countries under much the same plan of operations. As the result of a cordial invitation in 1913 from the British colonial authorities to the International Health Board, co-operative campaigns were undertaken in British Guiana, Antigua, Trinidad, St. Lucia, Grenada, and Egypt. In Panama, Nicaragua, Costa Rica, Salvador, and Guatemala work was also subsequently undertaken on government invitation. This extension of control activities served in turn to stimulate investigation by such central bodies as the London School of Tropical Medicine and the Institut für Schiffs- und Tropenkrankheiten zu Hamburg, not to mention the excellent work done quite independently on various estates in the Dutch East Indies.

By 1915 the hookworm work of the International Health Board had been extended to ten Southern States and thirteen foreign countries, and by 1916 to the same number of states and fifteen foreign countries. Although in certain countries active work was later discontinued on account of the war, it was in most cases resumed soon after the close of the war, so that at the end of 1921 effort was going forward in forty-one states and countries, including Jamaica, Porto Rico, St. Lucia, Trinidad, Costa Rica, Guatemala, Nicaragua, Panama, Salvador, Brazil, Colombia, Dutch Guiana, Australia, late German New Guinea, Papua, British North Borneo, Ceylon, India, and Siam. Nearly 4,000,000 people had been examined for hookworm disease in these various regions, including the Southern States, and over 2,000,000 had been found infected and treated, with the result that they were either greatly benefited or entirely cured. About one-third of the cases dealt with were in the Southern States; of the others the bulk were inhabitants of the West Indies, Central or South America, and the East.

In practically all the countries sanitary regulations have been enacted and a distinct impulse has been given to prophylaxis, especially along educational lines leading to the prevention of soil pollution; the medical profession and public-spirited laymen have become interested; and the effort to treat the people for the parasites has served in turn to give a distinct stimulus to scientific investigation of the disease as well as to the organization of permanent health departments.

## Efforts to Discover the Ideal Anthelmintic

Although other remedies for the treatment of hookworm disease—among them beta-naphthol, chloroform, and eucalyptus—had been tried at various times and places, thymol continued the drug of choice until 1917. How-

ever, the successful use of oil of chenopodium by Schüffner and Vervoort in Sumatra, beginning in 1900, indicated that this drug might prove at least as efficacious as thymol and might indeed possess some advantages that the latter remedy lacked. Comparative tests of the two drugs—begun in 1915 under both hospital and field conditions by the Uncinariasis Commission to the Orient, and later substantiated under strictly field conditions in Brazil and elsewhere—showed that oil of chenopodium in the maximum safe dose was slightly more powerful than thymol, while at the same time it was cheaper, easier to administer, and, in the minds of the patients, less unpleasant to take.

After these early experiments the drug sprang into widespread favor, and for the most part the results reported from its use were excellent. But it was soon found that the oil was subject to variations in strength and toxicity, so that during the past few years many investigators have been seeking not only to develop a better pharmacopeial standard for the chenopodium, but to test as well the advantages and disadvantages of certain other newer remedies.

# Greater Refinement in Methods of Diagnosis

By the previously described method of diagnosing hookworm disease—that of searching with the microscope for hookworm eggs in the feces—the eggs are not immediately apparent unless the infection is heavy. A great many refinements in the technique have therefore been made, not only to render diagnosis more accurate but also more expeditious. One such device is the centrifuge, which serves to bring about a greater concentration of eggs in the microscopic field.

Another process consists of adding to the specimen of feces, solutions of chemicals, such as salt brine, having a specific gravity considerably greater than that of the fecal preparation. The addition of various briny liquids causes the eggs to rise to the surface, where they may be examined without removal, or may be first removed and then examined. Other methods cause the eggs to sink, so that they may be collected from the sediment. These newer techniques, depending, as the case may be, upon flotation or sedimentation, are known by various names, such as the Lane levitation, the glycerin-salt, and the brine-flotation-loop method."

## Mass Treatment of Heavily Infected Population

Of late years, in certain heavily infected tropical countries, it has become customary to dispense altogether with preliminary fecal examination. In such regions practically every person is known to be infected, and the people are treated *en masse* without preliminary diagnosis. The plan

was first tried on some of the estates in Java and elsewhere in the Dutch East Indies, and was later put to extensive use in Ceylon and Siam. It has also been used to a limited extent in Brazil. One of the reasons for its adoption lies in the fact that it is coming to be recognized that in hookworm control the essential thing is not so much to aim at the absolute cure of every infected person in the community, as it is quickly to remove the largest possible number of worms from the largest possible number of persons, and thus lower the severity of infection.

#### Life of Hookworm Larvae

During the early years of anti-hookworm activity in Europe, attention centered on finding a disinfectant that would kill the parasite in its free or larval stage. It was thought that thorough disinfection of soil was the indicated method of control, inasmuch as the worms could not multiply within the human body, each worm having to make its way in separately from the outside. Unfortunately, however, the larva at its infective stage is extremely resistant to most of the ordinary chemicals, and the effort to find an effective disinfectant cheap enough for extensive use has thus far been unsuccessful. Even in such comparatively limited areas as were dealt with in the European campaigns, the idea of disinfection had to be abandoned. Nevertheless, even though in the main attention is now settled on other methods of control, such as the encouragement of latrine building, proper waste disposal, and the treatment of infected persons, investigations to determine the effect of chemicals on the larvae are still in progress; and in comparatively small or isolated "nests" of infection, as well as occasionally in latrines, limited use is being made of the principle of disinfection.

The question whether the digestive juices of animals will destroy ingested human hookworm larvae has also come up, with the result that in recent years some of the early theories on this point have been refuted. Scientific work has also been done to determine the rôle of domestic animals in the spread of the infection. Although not carriers of the human hookworm, many of these animals, such as pigs and chickens, which act as scavengers, may pass the infective larvae unharmed through their intestines, or carry them on their feet, and thus aid in their spread.

Both these questions are part of the larger problem of determining precisely what factors influence the life of hookworm larvae in the soil. It is known in a general way that air, warmth, and moisture are necessary for hatching hookworm eggs, and that desiccation and cold are two of the chief hindrances to the development of the eggs into dangerous, infective larvae. Progress in the investigation of this phase of the subject has

recently been made possible by the development of improved methods for recovering the larvae from the soil. A specimen of infected soil can now be taken from any place and its larval content determined with considerable accuracy, which makes possible a study of hookworm larvae in their natural habitat instead of merely in the laboratory. These and other scientific activities at present under way give promise of throwing considerable light on the points that remain in doubt.

## EXPLANATORY NOTES

An asterisk preceding an entry denotes an unpublished manuscript in the library of the Rockefeller Foundation.

The list of abbreviations of titles of periodicals follows, with few exceptions, the usage of the library of the Surgeon General of the United States Army.

The spelling of "ancylostoma" is based on the decision of the International Commission on Zoological Nomenclature.

References in French, German, Italian, and Spanish have not been translated. Translations of titles published in languages not so generally known have been appended.

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Apx A, B, incorporated in the report.

Apx C, Examination of the children of the primary schools of Panama city by Dr. F. C. Caldwell. 1921. 7p.

Apx D, Constructive analysis of a four years' campaign against the hookworm

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# ABBREVIATIONS OF TITLES OF PERIODICALS

Abeille méd., Par. Actas y trab. d. Cong. méd. ecuatoriano, Guayaquil Alabama M. J., Birmingham Alabama M. & S. Age, Birmingham Albany M. Ann. Alienist & Neurol., St Louis Alkaloid. Clin., Chic. Allg. med. Centr.-Ztg, Berl. Allg. Wien, med. Ztg Am. Chem. J., Balt. Am. Ency. & Dict. of Ophthal., Am. Health, N. Haven & N. Y. Am. J. Clin. M., Chic. Am. J. Dis. Child., Chic. Am. J. M. Sc., Phil.

Am. J. Obst., N. Y.

Am. J. Ophth., St. Louis Am. J. Otol. Am. J. Physiol., Bost. Am. J. Pub. Health

Am. J. Trop. Dis. (etc.) N. Orl.

Am. M. J., St Louis Am. M. Rev., N. Y. Am. Med.

Am. Pract. & News, Louisville Amazonas med., Manaos Amtsarzt, Leipz. & Wien An. d. Circ. méd. argent., Buenos Aires

An. del hosp. de San José, Costa An. r. Acad. de med., Madrid

An. Rept Sur. Gen. U. S. Army, Wash. An. Univ. centr. de Venezuela,

Ann. d. Accad. di agric. di Torino

Ann. Am. Acad. Pol. & Soc. Sc., Phil. Ann. et bull. Soc. de méd. de Ann. di chim. e di farm.

Abeille médicale. Paris Actas y trabajos del Congreso médico ecuatoriano. Guayaquil

Alabama Medical Journal. Birmingham Alabama Medical and Surgical Age. Birmingham

Albany Medical Annals, Albany Alienist and Neurologist. St Louis Alkaloidal Clinic. Chicago Allgemeine medicinische Central-Zeitung. Berlin Allgemeine Wiener medicinische Zeitung. American Chemical Journal. Baltimore Wien American Encyclopædia & Dictionary of Ophthalmology. Chicago

American Health. New Haven & New York American Journal of Clinical Medicine. Chicago American Journal of Diseases of Children. Chicago American Journal of the Medical Sciences. Philadelphia

American Journal of Obstetrics and Diseases of Women and Children. New York American Journal of Ophthalmology. St Louis American Journal of Otology. New York; St Louis American Journal of Physiology. Boston

American Journal of Public Health. New York: Boston; Chicago American Journal of Tropical Diseases and Pre-

ventive Medicine. New Orleans American Medical Journal. St Louis American Medical Review. New York American Medicine. Philadelphia; Burlington (Vt); New York

American Practitioner and News. Louisville (Kv) Amazonas medico. Manáos

Amtsarzt. Leipzig & Wien Anales del Círculo médico argentino. Buenos Aires

Anales del hospital de San José. Costa Rica

Anales de la real Academia de medicina, Madrid. Annual Report of the Surgeon General United States Army. Washington

Anales de la Universidad central de Venezuela. Carácas

Annali dell' Accademia di agricoltura di Torino. Torino

Annals of the American Academy of Political and Social Science. Philadelphia Annales et bulletin de la Société de médecine de

Gand. Gand Annali di chimica e di farmacologia. Bologna;

Milano

Ann. d. Fac. di med., Perugia

Ann. d'hyg., Par.

Ann. d'hyg. et de méd. colon., Par.

Par.
Ann. d'ig., Roma
Ann. d'ig., sper., Roma
Ann. de l'Inst. Pasteur, Par.
Ann. di Ippocrate, Milano
Ann. d. Ist. Maragliano p. la
cura d. tuberc. (etc.) Genova

Ann. di med. nav., Roma Ann. d. mines: pte administra-

tive . . . lois, décrets, etc., Par.

Ann. d. mines: ou Recueil des mem., Par.

Ann. d. mines de Belg., Brux. Ann. Museo civ. d. Genova Ann. d'ocul.

Ann. di ostet.

Ann. d. ottal.

Ann. paulist. de med. e cirurg., S. Paulo

Ann. Soc. de méd. d'Anvers

Ann. Soc. de méd. de Gand Ann. Soc. de méd. de St-Étienne et de la Loire, St-Étienne Ann. Soc. méd.-chir. d'Anvers

Ann. Soc. méd.-chir. de Liége

Ann. Soc. oy. d. sc. méd. et nat.
de Brux.

Ann. d. travaux pub. de Belg., Brux.

Ann. Trop. M. & Parasitol., Liverp. Ann. d. Univ. libera di Perugia Ann. univ. di med. e chir.,

Milano Annuario d. sc. med., Milano Antiseptic, Edinb. & Madras Arb. a. d. k. Gsndhtsamte, Berl.

Arch. f. Anat. u. Physiol., Leipz. Arch. f. Augenh., Wiesb.

Arch, de biol,

Arch. brasil. de metl., Rio de Jan. Arch. brasil. de psychiat. (etc.) Rio de Jan.

Arch: f. Chem. u. Meteorel., Nürmbg

Arch. Diagn., N. Y.

Arch. f. exper. Path. u. Pharmakol., Leipz.

Annali della Facoltà di medicina, Università di Perugia. Perugia

Annales d'hygiène publique et de médecine légale. Paris

Annales d'hygiène et de médecine coloniales. Paris

Annali d'igiene, pubblicazione mensile. Roma Annali d'igiene sperimentale. Roma Annales de l'Institut Pasteur. Paris Annali di Ippocrate. Milano

Annali di Ippocrate. Milano Annali dell' Istituto Maragliano per lo studio e la cura della tuberculosi (etc.) Genova

Annali di medicina navale e coloniale. Roma Annales des mines: partie administrative ou Recueil des lois, décrets. Paris

Annales des mines: ou Recueil des mémoires. Paris

Annales des mines de Belgique. Bruxelles Annales Museo civico di venova. Genova Annales d'oculistique. Bruxelles; Paris Annali di ostetricia e ginecologia. Milano; Firenze Annali di ottalmologia. Milano; Pavia

Annaes paulistas de medicina e cirurgia. São Paulo

Annales et bulletin de la Société de médecine d'Anvers. Anvers

Annales de la Société de médecine de Gand. Gand Annales de la Société de médecine de St-Étienne et de la Loire. St-Étienne

Annales de la Société médico-chirurgicale d'Anvers. Anvers

Annales de la Société médico-chirurgicale de Liége Liége

Annales de la Société royale des sciences médicales et naturelles de Bruxelles. Bruxelles Annales des travaux publics de Belgique. Bruxelles

Annals of Tropical Medicine and Parasitology. Liverpool Annali dell' Università libera di Perugia. Perugia

Annali universale di medicina e chirurgia. Milano Annuario delle scienze medica. Milano Antiseptic. Edinburgh & Madras

Arbeiten aus dem kaiserlichen Gesundheitsamte. Berlin Archiv für Anatomie und Physiologie. Leipzig Archiv für Augenheilkunde. Wiesbaden Archives de biologie. Gand; Liége & Paris Archivos brasileiros de medicina. Rio de Janeiro Archivos brasileiros de psychiatria, neurologia e sciencias affins. Rio de Janeiro

Archiv für Chemie und Meteorologie. Nürmberg

Archives of Diagnosis. New York
Archiv für experimentelle Pathologie und Pharmakologie. Leipzig

Arch. di farmacol. sper., Roma

Arch. gén. de méd., Par.
Arch. d. Heilk., Leipz.
Arch. de hig. e path. exotic.,
Lisb.
Arch. de l'Inst. Pasteur, Tunis
Arch. Int. Med., Chic.
Arch. internat. de pharmacod.,
Gand et Par.
Arch. ital. de biol.

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Stuttg.
Arch. Pub. Health Lab., Univ.

Manchester Arch. d. sc. biol (etc.) St-Pétersb.

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Arch. f. Schiffs-u. Tropen-Hyg., Leipz.

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Berl. Klinik

Biochem. Ztschr., Berl. Biol. Centralbl.

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Bol. Dir. de salubridad pub., Lima

Bol. Lab. munic., Guayaquil

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Atti della reale Accademia dei Lincei: Transunti Roma

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Boletín del Dirección de salubridad pública. Lima

Boletín de Laboratorio municipal. Guayaquil

Bol, de med, y cirug., Guayaquii Boll. d. clin. Boll. dell' emigraz., Roma Boll. d. mus. di zool. (etc.) Boll, d. r. Accad. med. di Genova Roll, d. sc. med., Bologna Boll, d. Soc. adriatica di sc. nat. in Trieste Boll. Soc. d'ig. di Palermo Boll, d. Soc. Lancisiana d. osp. di Koma Boll, d. Soc. med. di Parma Loll, d. Soc. med.-chir. di Pavia, Boll, d. Soc. rom. per gli stud. zool., Roma Boll, d. Soc. zool. ital., Roma Boston M. & S. J. Brazil-med., Rio de Tan. Brit. Guiana M. Ann., Demerara Brit. M. J., Lond. Brooklyn M. J. Budanesti orv. ujság Buffalo M. J. Bull. Açad. de méd., Par. Bull. Acad. roy. de méd. de Belg., Brux. Bull. Atlanta.M. Col. Bull. d. comitato med. cremonese. Cremona Bull. Entomol. Research, Lond. Bull. de l'Inst. Pasteur, Par. Bull. internat. Acad. d. sc. de Cracovie Bull. Internat. Ass. M. Mus. Bull. Internat. Labor off. Bull. Kentucky M. Ass., Louisville Bull. méd., Par. Bull. méd. de l'Algérie, Alger Bull. méd. du nord, Lille Bull. et mém. Soc. méd. d. hôp. de Par. Bull. et mém. Soc. de thérap., Bull. mens. d. Accad. di sc. nat. in Catania Bull. de l'Office internat. d'hyg. pub., Par. Bull. Pan-Am. Union, Wash.

Bull. d. r. Accad. med. di Roma

Boletín de medicina y cirugía. Guayaquil Bollettino delle cliniche. Napoli; Milano Bollettino dell' emigrazione. Roma Bollettino dei musei di zoologia e anatomia comparata della r. Università di Genova. Genova Bollettino della r. Accademia medica di Genova. Genova Bollettino delle scienze mediche di Bologna. Bologna Bollettino della Sociteà adriatica di scienze naturali in Trieste. Trieste Bollettino della Società d'igiene di Palermo. Palermo Bollettino della Società Lancisiana degli ospedali di Roma. Roma Bollettino della Società medica di Parma. Parma Bollettino della Società medico-chirurgica di Pavia. Bollettino della Società romana per gli studi zoologici. Roma. Bollettino della Società zoologica italiana. Roma Boston Medical and Surgical Journal. Boston Brazil-medico. Rio de Janeiro British Guiana Medical Annual and Hospital Demerara Reports. British Medical Journal. London Brooklyn Medical Journal. Brooklyn (N. Y.) Buda pesti orvosi ujság. Budapest Buffalo Medical Journal. Buffalo Bulletin de l'Académie de médecine. Bulletin de l'Académie royale de médecine de Belgique. Bruxelles Bulletin Atlanta Medical College. Atlanta (Ga.) Bullettino del comitato medico cremonese. Cremona Bulletin of Entomological Research. London Bulletin international de l'Académie des sciences de

Bulletin de l'Institut Pasteur. Paris Cracovie: Comptes rendus des séances. Cracovie Bulletin of the International Association of Medical Museums. Washington; Ann Arbor Bulletin of the International Labor Office. Basel: Bulletin Kentucky State Medical Association. Louisville (Kv) Bulletin médical. Paris Bulletin médical de l'Algérie. Alger

Bulletin médical du nord. Lille Bulletins et mémoires de la Société médicale des hôpitaux de Paris. Paris Bulletins et mémoires de la Société de thérapeutique. Bullettino mensuale della Acçademia di scienze naturali in Catania. Catania Bulletin de l'Office international d'hygiène publique. Bulletin of the Pan-American Union. Washington (D. C.)

Bullettino della reale Accademia medica di Roma. Roma

Bull, d. sc. pharmacol., Par.

Bull. d. schweiz. Gsndhtsamtes Bull. d. sedute d. Accad. Gioenia di sc. nat. in Catania

Bull. Soc. anat. de Par. Bull. Soc. centr. de méd. vét., Par.

Bull Soc. clin. de Par.

Bull. Soc. de l'industrie miner., St-Etienne

Bull. d. Soc. Lancisiani d. osp. di Roma

Bull. Soc. linnéenne de Normandie, Caen

Bull. Soc. méd. de Charleroi

Bull. Soc. méd. pub. et d'hyg. prof., Par.

Bull. Soc. méd. de la Suisse romande, Lausanne

Bull. Soc. nat. d'acclimatation de France, Par. Bull. Soc. d'ophtal. d'Égypte,

Cairo

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Roma
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Roma Giornale della reale Accademia di medicina di Torino. Torino Giornale della reale Società italiana d'igiene. Milano Giornale della Società fiorentina d'igiene. Firenze

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Zeitschrift für das Berg-Hütten-und Salinenwesen im preussischen Staate. Berlin

Zeitschrift für Gewerbe-Hygiene, Unfall-Verhütung und Arbeiter-Wohlfahrts-Einrichtungen. Zeitschrift für Heilkunde. Berlin; Wien

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